March 19, 2001

PEER REVIEW CHARGE

Introduction

The U.S. Environmental Protection Agency (EPA) has asked Industrial Economics, Incorporated for assistance in conducting a peer review of the scientific basis supporting the health hazard and dose response assessments for phenol, which will be used in the Agency's Integrated Risk Information System (IRIS). This document provides related information for the peer reviewers. Materials to be reviewed include the *Toxicological Review*, which will also be made available to the public, and the studies that were identified as critical for the development of the RfD. Below, we provide background information pertaining to the project, the goal of the review, a list of general and specific questions to be addressed in the review, and guidance for articulating your overall recommendation.

Background

The goal of the project is to review the hazard and dose-response assessments for phenol, which were developed based on the following Agency guidelines and methodologies: *The Risk Assessment Guidelines* (1986), the (new) guidelines for *Carcinogen Risk Assessment* (1996), *Guidelines for Developmental Toxicity Risk Assessment* (proposed), *Interim Policy for Particle Size and Limit Concentration Issues in Inhalation Toxicity* (proposed), *Guidelines for Neurotoxicity Risk Assessment*, *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry*, *Recommendations for and Documentation of Biological Values for Use in Risk Assessment*, and *Use of the Benchmark Dose Approach in Health Risk Assessment*. We will provide copies of these documents (and/or relevant sections) upon request. The studies specific to phenol are referenced in the *Toxicological Review*, and copies of the critical studies are included with this Charge.

Once EPA evaluates and addresses the peer review comments, the assessment will be subject to EPA's Consensus Process for final approval and adoption. These hazard and dose-response assessments will then appear on IRIS and become available as Agency consensus health effect information.

Review Goal

The primary function of the peer reviewer should be to judge whether the choice, use, and interpretation of data employed in the derivation of the assessment is appropriate and scientifically sound. This review is not of the recommended Agency risk assessment guidelines or methodologies used to derive cancer or RfD/C assessments as these have been reviewed by external scientific peers, the public, and EPA Science Advisory Boards. The reviewer's comments on the application of these

guidelines/methodologies within the individual assessments are, however, welcomed and encouraged. For example, the reviewer may ascertain whether or not there is data sufficient to support use of other than default assumptions for areas such as sensitive subpopulations. The reviewer may also have opinions on other areas of uncertainty such as subchronic to chronic duration (when only subchronic study is available) or an incomplete data base but should focus on the specific area of uncertainty rather than on the magnitude of the overall estimate.

Below are two groups of questions regarding this review. The first is a set of general questions that are meant to guide you through your review. It is not imperative that you specifically answer each question in this group. The second group of questions, however, are specific for the phenol assessment and deal with areas of scientific controversy or uncertainty in which the Agency may have to make a scientific judgment. Your responses to these questions are vital to the review process.

Charge for Phenol Peer Reviewers

While reviewing the document, please address the following general issues.

1. Comment on the organization of the *Toxicological Review* document. Does the document present the information in a clear, concise, and easy to follow format? If not, please provide suggestions to improve the presentation.

2. Are you aware of any other data/studies that are relevant (i.e., useful for the hazard identification or dose-response assessment) for the assessment of the adverse health effects, both cancer and noncancer, of this chemical?

3. For the RfD, has the most appropriate critical effect been chosen (i.e., that adverse effect appearing first in a dose-response continuum)? Relevant to human health? Points relevant to this determination include whether or not the choice follows from the dose-response assessment, whether the effect is considered adverse, and if the effect (including tumors observed in the cancer assessment) and the species in which it is observed is a valid model for humans.

4. Has the noncancer assessment been based on the most appropriate studies? These studies should present the critical effect/cancer (tumors or appropriate precursor) in the clearest dose-response relationship. If not, what other study (or studies) should be chosen and why?

5. For the noncancer (RfD) assessment, are there other data that should be considered in developing the uncertainty factors or the modifying factor? Do you consider that the

data support use of different (default) uncertainty factors than those proposed?

6. Do the confidence statements and weight-of-evidence statements present a clear rationale and accurately reflect the utility of the studies chosen, the relevancy of the effects (cancer and noncancer) to humans, and the comprehensiveness of the data base? Do these statements make sufficiently apparent all the underlying assumptions and limitations of these assessments? If not, what needs to be added?

In addition, the following specific issues should be addressed.

1. When endogenously produced phenol is taken into account, is the RfD supportable? Note that the RfD is applied to ingested phenol in addition to the normal daily endogenously produced phenol. Are there differences in endogenous phenol production between rats and humans that should be taken into account in the development of the RfD?

2. Do you agree/disagree with the recommendation that there are not sufficient data to generate a scientifically defensible RfC and cancer slope factor?

3. Was the interpretation of the decreased fetal body weight in rats in the National Toxicology Program (NTP) study (NTP, 1983a) appropriate?

4. Please comment on the choice of gavage developmental toxicity studies as the co-critical studies in light of the differences between phenol toxicity when administered in drinking water and by gavage.

5. Was the interpretation of decreased motor activity in the 13-week oral neurotoxicity study appropriate?

Recommendations

Based on your reading and analysis of the information provided, please identify your overall recommendation regarding the *Toxicological Review* using one of the following statements:

- acceptable as is;
- acceptable with minor revision (as indicated);
- acceptable with major revision (as outlined); or
- not acceptable.